Evaluating trends in HIV/HBV Co-infection prevalence in the era of HBV-active antiretroviral therapy

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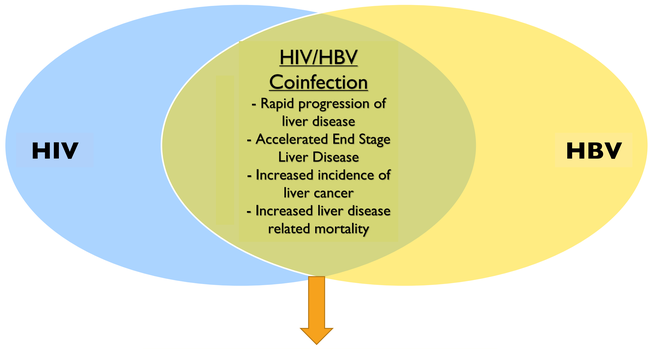
Background



In Nigeria…

3 million people living with HIV

20 million people living with chronic HBV

HIV/HBV co-infection prevalence: **11-17.8%**

Given the clinical importance and significant burden of HIV and chronic HBV in Nigeria, it is important to understand more about epidemiological trends of HIV/HBV co-infection in this setting.

Question & Hypothesis

What is the trend in HIV/HBV coinfection prevalence in Nigeria over the past ~15 years?

Four main factors

1. Changing paradigms of transmission
In locations where the carrier rate for HBV is >8% the predominant mode of infection is vertical (mother to child)
However, emerging evidence suggests sexual transmission as the major mode of transmission of HBV among HIV-infected adults in Africa (Calisiti et al 2015).

2. Introduction of the dual HBV active ARVs (2010)
HBV-active ART (tenofovir plus emtricitabine or lamivudine) leads to high rates of HBV virologic suppression

New evidence suggests introduction contributing to a decline in **HBV incidence** in HIV-infected individuals in other African countries (Chun et al 2010)

→ Could this also contribute to decreased **prevalence among** co-infected individuals via decreased sexual transmission

3. HIV Prevention programs (PMTCT and other)

4. Introduction of HBV vaccination for infants (2004)

We **hypothesize** that the **prevalence of HBV has significantly declined** among HIV-infected patients in the era of ART scale up, through a combination of behavioral changes induced by **AIDS prevention programs**, the use of **dual HBV-active ART**, and introduction of the **HBV vaccination** for infants which was rolled out in 2004.

Methods

Study subjects: All HIV-infected Nigerian adults (>18) enrolled at the APIN Public Health Initiatives-supported HIV clinic at Jos University Teaching Hospital from 2004-2018

Inclusion criteria: HBsAg + at time of HIV diagnosis or entry into APIN program; ART naive
Exclusion criteria: a) undocumented HIV diagnosis; b) unknown HBsAg status at time of entry;

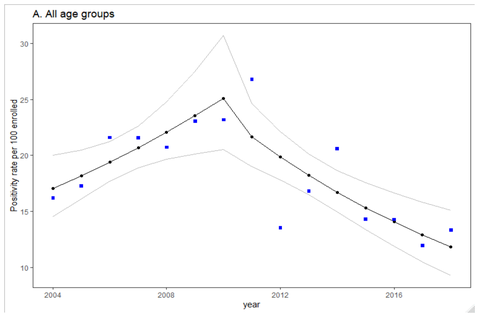
Modeled count data using negative binomial or quasi-poisson regression with offset for number of tests per year. Calculated yearly cross section – HBsAg of newly enrolled each year.

Results

Table 1: Baseline characteristics of study cohort

	Overall	HBsAg Negative	HBsAg Positive
Total	21585	17255	4330
Age (mean (SD))	35.15 (9.42)	35.28 (9.54)	34.62 (8.91)
Male sex (%)	7545 (35.0)	5885 (34.1)	1660 (38.3)
Education (%)			
No education	3714 (17.2)	3025 (17.5)	689 (15.9)
Primary	4376 (20.3)	3502 (20.3)	874 (20.2)
Secondary	6831 (31.6)	5415 (31.4)	1416 (32.7)
Tertiary	6664 (30.9)	5313 (30.8)	1351 (31.2)
Ever married (%)	16910 (78.3)	13627 (79.0)	3283 (75.8)
Year tested (%)*			
2004	1301	1090 (84%)	211 (16%)
2005	3581	2961 (83%)	620 (17%)
2006	4928	3862 (78%)	1066 (22%)
2007	3443	2696 (78%)	747 (22%)
2008	2146	1698 (79%)	448 (21%)
2009	1749	1348 (77%)	401 (23%)
2010	789	607 (77%)	182 (23%)
2011	757	555 (73%)	202 (27%)
2012	625	540 (86%)	85 (14%)
2013	885	736 (83%)	149 (17%)
2014	486	386 (79%)	100 (21%)
2015	357	307 (86%)	50 (14%)
2016	137	118 (86%)	19 (14%)
2017	257	226 (88%)	31 (12%)
2018	144	125 (87%)	19 (13%)

Figure 1: HBsAg positivity rate for all age groups from 2004-2018.



Term "positivity rate" on y axis is interchangeable with "prevalence per year" to describe the trend of yearly prevalence of coinfection through time

- **HBsAg positivity increased over time until it declined at a break point of 2010 (Figure 1)**
- **Post-2010 declines were less pronounced in the older age groups compared to others (Fig 2-4)**

Figure 2: HBsAg positivity rate for age <30 from 2004-2018

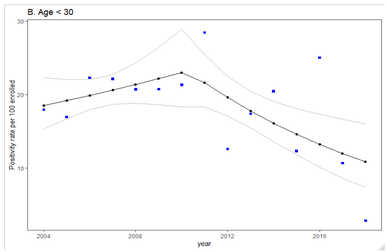


Figure 3: HBsAg positivity rate for age 30-40 from 2004-2018

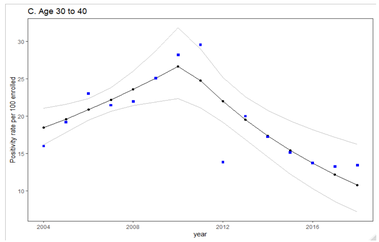


Figure 4: HBsAg positivity rate for age 40-50 from 2004-2018

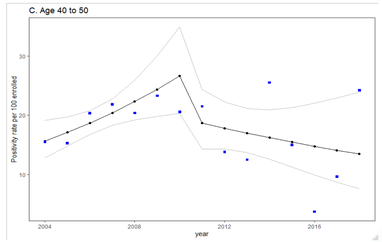
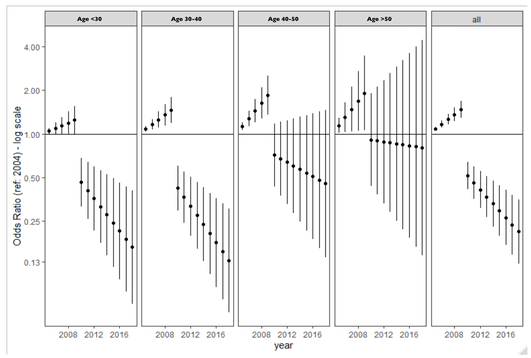


Figure 5: Odds of annual HBsAg positivity vs. 2004, by age group.



- **Odds ratio testing was performed to assess how prevalence changed overtime, by age group**
- **The odds of being HBV co-infected drop off significantly after 2010**

TAKE AWAY

Co-infection with HBV increased over time until 2010 when it declined significantly

This breakpoint is correlated with the introduction of dual HBV active ART

Table 2: Risk factors associated with HBsag positivity, by age group

	Population: all age groups		Population: <30 years old		Population: 30 - 40 years old		Population: 30 - 40 years old		Population: >50 years old	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age group										
30 to 40	1.06 (0.97 to 1.15)	0.19	n.i.		n.i.		n.i.		n.i.	
40 to 50	0.91 (0.82 to 1.01)	0.08	n.i.		n.i.		n.i.		n.i.	
> 50	0.72 (0.61 to 0.84)	<0.01	n.i.		n.i.		n.i.		n.i.	
Male (vs Female)	1.25 (1.16 to 1.35)	<0.01	1.24 (1.07 to 1.43)	<0.01	1.35 (1.21 to 1.5)	<0.01	1.17 (0.99 to 1.39)	0.06	0.9 (0.66 to 1.23)	0.53
Primary	1.06 (0.95 to 1.19)	0.29	1.12 (0.92 to 1.35)	0.24	1.08 (0.9 to 1.3)	0.43	1.02 (0.79 to 1.33)	0.86	0.95 (0.63 to 1.41)	0.79
Secondary	1.08 (0.97 to 1.2)	0.16	1.15 (0.97 to 1.37)	0.10	1.04 (0.88 to 1.24)	0.63	1.03 (0.79 to 1.34)	0.83	0.99 (0.62 to 1.59)	0.97
Tertiary	1.06 (0.96 to 1.18)	0.26	1.04 (0.86 to 1.26)	0.70	1.02 (0.85 to 1.22)	0.83	1.29 (1.02 to 1.62)	0.03	0.9 (0.61 to 1.33)	0.60
Ever married (vs never)	0.87 (0.79 to 0.94)	<0.01	0.85 (0.75 to 0.96)	<0.01	0.88 (0.77 to 1.02)	0.08	0.85 (0.58 to 1.24)	0.39	0.37 (0.15 to 0.94)	0.03

TAKE AWAY

- **Less likely to be HBsAg positive if >50**
- **Males more likely to be positive**
- **Ever married less likely to be positive**
- **Education not a predictor***

Conclusions

- The decline in HIV/HBV co-infection prevalence after the introduction of HBV-active ART as well as the higher prevalence rates observed among men and unmarried individuals, suggest that **sexual transmission could be a more significant source of HBV transmission in African settings than previously thought.**
- Just as decreased incident risk of HBV has been reported in several HIV cohorts after initiation of HBV active ART**, we found a decline in HBV coinfection prevalence rates after 2010 which suggests a possible direct relationship between the population level use of HBV active ART introduced in 2010, the sexual transmission of HBV, and the prevalence of coinfection.**
- Declines in behavioral risks associated with HBV in Nigeria such as tribal scarification, sharing sharp objects, and 'traditional' circumcision may have also contributed to these declines (Adebola O et al. AJTMH 2016)
- Given the relatively late introduction of infant HBV vaccination (2004) in Nigeria, it is unlikely that increased uptake of vaccine contributed to these declines.

➢ **HBV active ART & routine screening of HIV-infected patients for HBV is essential in treating HIV/HBV coinfected populations & can greatly decrease liver disease morbidity and mortality**

Caveats & Future Directions

Caveats:

- Various possible confounders for drop off in 2010, including sample size reduction

Future directions:

- Next aims of the grant: Examine the utility of qHBsAg measurement in HIV/HBV co infected patients on HBV-active therapies

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